

CLAIMS

1. A method for the production of micropellets comprising one or more hard to dissolve effective agents, in which micronized particles are produced from dispersions with functional adjuvants for the formation of a solid dispersion of the particles by spray granulation in a fluidized bed process, with the functional adjuvants and other components for the formation of the micropellets being provided in a dissolved or dispersed form.
2. A method according to claim 1, characterized in that a weight ratio of the functional adjuvants for formation of the solid dispersion to the effective agent ranges from 20:1 to 1:100, for example from 5:1 to 1:10.
3. A method according to one of claims 1 or 2, characterized in that the effective agent is provided in a micronized form with a grain size of 30 μm or less, in particular between 0.1 and 30 μm .
4. A method according to one of claims 1 through 3, characterized in that one or more solutizers are provided as functional adjuvants for the formation of the solid dispersion, in particular one or more polyoxypropylene polyoxyethylene condensates, fatty acid polyglycol ether, alkyl phenol polyethylene glycolether, triglycerides, anionic tensides, cationic tensides, amphoteric detergents or non-ionic tensides, or preferably a polyoxypropylene oxyethylene (block)polymerisate.
5. A method according to one of claims 1 through 4, characterized in that one or more effective agents are provided as the hard to dissolve effective agents, selected from macrolide antibiotics, in particular azithromycin, antiviral therapeutics which are hard to dissolve in water, analgetics which are hard to dissolve in water, cardiovascular medications which are hard to dissolve in water, antiphlogistics which are hard to dissolve in water, and cancer therapeutics which are hard to dissolve in water.

6. A method according to one of claims 1 through 5, characterized in clarithromycin being provided as the hard to dissolve effective agent.

7. A method according to one of claims 1 through 5 or 6, characterized in that the solid matter to be pelletized is provided as a liquid dispersion, comprising the micronized effective agent and perhaps functional adjuvants for the formation of a solid dispersion and a desired binder, injected from a bottom into a fluidized bed arrangement which is empty at a beginning of the process;

starting seeds for pelletizing being formed by way of spray granulation of the dispersion without the presence of any other inert material; and

the micropellets produced during the process being sifted via a classification device, in particular an air separator, primarily a zigzag-separator, and being removed from the separator when reaching a predetermined pellet size.

8. A method for the production of a dispersion of a micronized effective agent, characterized in that

in a first separate step, a homogenous suspension of the micronized effective agent is produced in water, by suspending the micronized, hard to dissolve, in particular not water-soluble effective agent, several respective effective agents or a respective mixture of effective agents being suspended by way of a powder-wetting or dispersing device and by a mixer for homogenizing and/or deaerating the dispersion in water under deaeration and homogenization;

in another separate step, a solution of the soluble (in particular water-soluble) functional adjuvants and other components for the formation of micropellets as defined in claims 1 through 6 is mixed in a solvent, until the solution becomes clear;

and the dispersion of the first step and the homogenous solution of the other step are mixed with one another and deaerated in a subsequent step such that a homogenous liquid dispersion develops, advantageously by way of powder wetting or dispersing devices, with the homogenous solution being introduced by the device and mixed with the dispersion containing the effective agent and the mixture and the deaeration being simultaneously carried out by a jet stream mixer.

9. A method according to one of claims 1 through 5, 7 or 6, characterized in that a dispersion produced according to claim 7 is nebulized in a fluidized bed evaporator, with the solvent being removed during a drying process through evaporation.
10. Micropellets produced according to the method according to one of claims 1 through 5, 7, 6, or 9.
11. Micropellets according to claim 10, comprising the following components:
- (i) the pharmacological effective agent in a micronized form at a ratio from 10 through 99 %, preferably 20 through 90 % by weight;
 - (ii) the functional adjuvants for the formation of a solid dispersion at a ratio from 1 through 90 % by weight, preferably from 1 through 50 % by weight, and
 - (iii) preferably a binder at a ratio from 0 to 20 % by weight, for example from 5 to 15 % by weight.
12. Micropellets according to one of claims 10 or 11 having a diameter from 0.1 to 500 μm , preferably in spherical form.
13. Micropellets according to one of claims 10 through 12, characterized in that no more than 25 % by weight of the pellets have a diameter deviating by more than 25 % (+/-) from a mean diameter of all of the pellets.
14. A pharmaceutical formulation comprising micropellets according to one of claims 10 through 13.
15. A method for producing coated micropellets, comprising the production of a micropellet according to one of claims 1 through 5, 6, 7, or 9, characterized in that after the production of the pellets according to one of claims 1 through 5, 6, 7, or 9 in a subsequent step a coating is preferably also performed in a fluidized bed process, with

nozzles in a base atomizing a coating fluid, in which the coating agents are dissolved or emulgated, in a parallel flow into the micropellets to be coated.

16. A method according to claim 15, characterized in that after a first internal protective coating, subsequently (in the same charge or after an interim isolation of the interim product, i.e. once coated micropellets) one or more coatings are applied.

17. Coated micropellets, produced according to the method according to one of claims 15 or 16.

18. Coated micropellets according to claim 17, provided with two coatings, in particular, an inner protective coating and an outer coating resistant to gastric juice.

19. Coated micropellets according to one of claims 17 or 18, characterized in that within 15 minutes the micropellets show a release in effective agent of 75 % or more in a US paddle test at 75 rpm in a solution with pH of 6.8 or higher.

20 A pharmaceutical formulation, comprising a coated micropellet according to one of claims 17 or 18.